DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Tracking Form for Applicants for New Technology Add-on Payments under the Acute (for the complete application requirements, please see the instructions at http://cms.hhs.gov/providers/hipps/default.asp)

Note: The information provided on this tracking form may be made publicly available

1. **Applicant Name:** Guilford Pharmaceuticals, Inc. **Date:** October 24, 2002
2. **Manufacturer Name:** Guilford Pharmaceuticals, Inc.
3. **Contact Name:** Francesca Cook
4. **Address:** 6611 Tributary Street, Baltimore, MD 21224
5. **Telephone Number:** (410) 637-6307
6. **Email Address:** cookf@guilfordpharm.com
7. **Trade Brand of Technology:** GLIADEL® Wafer
8. **Brief Description of Service or Device:** GLIADEL® Wafer (polifeprosan 20 with carmustine implant) is a sterile, off-white to pale yellow wafer approximately 1.45 cm in diameter and 1 mm thick. Each wafer contains 192.3 mg of a biodegradable polyanhydride copolymer and 7.7 mg of carmustine [1,3-bis (2-chloroethyl)-1-nitrosourea, or BCNU]. Carmustine is a nitrosourea oncolytic agent. The copolymer, polifeprosan 20, consists of poly[bis(p-carboxyphenoxy) propane: sebacic acid] in a 20:80 molar ratio and is used to control the local delivery of carmustine. Carmustine is homogeneously distributed in the copolymer matrix.

   GLIADEL® Wafer is indicated for use as an adjunct to surgery to prolong survival in patients with recurrent glioblastoma multiforme (GBM) for whom surgical resection is indicated. Implanted directly into the cavity that is created when a brain tumor is surgically removed, GLIADEL® Wafer directly delivers anti-tumor medication to the site of the removed tumor.

New Criteria

9. **Date of FDA approval (or expected approval) for the device or service:** September 23, 1996
10. **Was the service or technology considered under FDA priority review?** Yes, GLIADEL Wafer was considered under priority review for both the recurrent and primary indications.
11. **Does the technology have an ICD-9-CM code or is one pending? If yes, please specify.** A new ICD-9-CM code -- 00.10 – implantation of a chemotherapeutic agent went into effect October 1 of this year.
12. **Does the service or technology have a HCPCS code associated with it? If yes, please specify.** No. See comments in full application.
13. **If the technology is a device, is there an IDE number assigned to the device? If yes, please specify.** The product is not a device.
14. **Have you submitted an outpatient application for pass-through payments under the Medicare outpatient prospective payment system? If so, when? Have you been approved? If yes, when was your approval?**
    No. The product is only used in the inpatient setting.

Cost Criteria

15. **Affected diagnosis-related groups (DRGs):** DRG 2
16. **What is the anticipated volume of this technology (by DRG)?** Approximately, 650 cases.
17. **Weighted standard deviation threshold in affected DRGs:** $34,673
18. **What is the anticipated average standardized charge per case involving this new technology?** FY 2003 average standardized charge is $36,093. See exhibit 5 of application.
19. **What is the estimated cost per case for the service or technology?** FY 2003 estimated cost is $22,763. See exhibit 3 of application.
20. **Number of cases/patients, distinguishing between Medicare and non-Medicare:** All of the patients in our data set are Medicare beneficiaries.
21. **Average dosage/number of units and estimated costs for sub-populations:** The average dose is eight wafers. The 2003 average wholesale price for a box of eight wafers is $10,985.

Clinical Improvement

22. Please provide a short synopsis of the following clinical issues added to the new technology. Use the regular application to submit full details.

    a. **Briefly describe how the new service or technology represents a substantial clinical improvement over existing services or technologies:**

GLIADEL® Wafer is the only implantable chemotherapy approved for malignant glioma and thus has few direct competitors. It has been associated with a reduction in the risk of death of 27% in the primary setting (p=.018) and 33% in the recurrent setting (p=.006). Improved survival associated with systemic chemotherapy provides only a 15% reduction in the risk of death (p<.0001).

b. **Briefly describe relevant clinical trial(s), including dates and findings:**

Registration Trial

Recurrent: March 1989 – September 23
A 222 patient Phase III, multicenter, placebo-controlled trial was conducted to assess the safety and efficacy of GLIADEL® Wafer in recurrent surgery for GBM. The recurrent surgery data demonstrated a hazard ratio of .67 representing a 33% decrease in the risk of death among GLIADEL® Wafer patients (p=.006). Median survival was increased by 33% in the GLIADEL® Wafer group when compared to placebo (31 vs. 23 weeks).

Primary: December 1997 – June 2000
A phase III, randomized, double-blind, placebo-controlled study conducted at 38 centers in 14 countries. The primary surgery data demonstrated a 29% percent reduction in the risk of death in GLIADEL® Wafer patients. The median survival in the GLIADEL® Wafer group was 13.9 months compared to 11.6 months in the placebo group (p=0.03).

c. List of published peer-review articles relevant to the new service or technology:

Recurrent surgery articles (Attachment D):

- Brem H, Piantadosi S, Burger PC, Walker M, Selker R, Vick NA, Black K, Sisti M, Brem S, Mohr G, et al., "Placebo-controlled trial of safety and efficacy of intraoperative controlled delivery by biodegradable polymers of chemotherapy for recurrent gliomas." *Lancet* 1995 Apr 22;345(8956):1008-12;

  Trial period: March 1989 – September 1993

- Brem H, Mahaley MS Jr, Vick NA, Black KL, Schold SC Jr, Burger PC, Friedman AH, Ciric IS, Eller TW, Cozzens JW, et al., "Interstitial chemotherapy with drug polymer implants for the treatment of recurrent gliomas." *J Neurosurg* 1991 Mar;74(3):441-6.

  Trial period: September 1987 – July 1988

Primary surgery articles *(Attachment E):*

- Westphal M, Delavault P, Hilt D, Olivares R, Belin V, Daumas-Duport C. "Placebo controlled multicenter double-blind randomized prospective Phase III trial of local chemotherapy with biodegradable carmustine implants (GLIADEL ™) in 240 patients with malignant gliomas: Final results." *Neuro-Oncology* 2000 Oct; 2(4):301 (abstract # 230).

  Awaiting publication in *Neuro-Oncology*, web access will be made available in November.

  Trial period: December 1997 – June 2000

- Valtonen S, Timonen U, Toivanen P, Kalimo H, Kivipelto L, Heiskanen O, Unsgaard G, Kuurne T. "Interstitial Chemotherapy with carmustine-loaded polymers for high-grade gliomas: a randomized double-blind study." *Neurosurgery* 1997 Jul;41(1):44-49.

  Trial period: March 1992 – March 1993

- Brem H, Ewend MG, Piantadosi S, Greenhoot J, Burger PC, Sisti M. "The safety of interstitial chemotherapy with BCNU-loaded polymer followed by radiation therapy in the treatment of newly diagnosed malignant gliomas: phase I trial." *Journal of Neuro-Oncology* 1995 Nov; 26(2):111-23.

  Trial period: July 1990 – August 1991

- "Long-term efficacy of local chemotherapy with biodegradable carmustine implants (GLIADEL® Wafer) in high-grade malignant gliomas." - On file Guilford. Has been submitted to the FDA and publication is expected next year.

  Trial period: December 1997 – August 16, 2002